REMARKS

Reconsideration of this application is respectfully requested.

Claims 1-51 were previously pending and are also being presented in this Response. No claims have been added, cancelled, or amended herein.

The First Rejection Under 35 U.S.C. §102(b)

Claims 1, 2, 4, 8, 12-14, 19 and 42-50 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Miller et al., BioChimie 67:769-776 (l985)

In the Office Action (page 3), the Examiner stated:

> Miller et al. discloses methyl phosphonate linked antisense oligos and their use in inhibition as antisense oligomers which reads on the instant claims. It is noted that the methyl phosphonates of the references are phosphodiesters in that they link between nucleotide residues via a set of esters (diesters) and contain phosphate and are thus included in the generic phosphodiester language of the instant claims regarding internal internucleoside linkages.

The anticipation rejection is respectfully traversed.

Applicants respectfully maintain that an identity of material elements is lacking between the instantly claimed invention and that of the cited Miller et al publication.

Reconsideration and withdrawal of the anticipation rejection is respectfully requested.

The Second Rejection Under 35 U.S.C. §102(b)

Claims 1-4. 12-14. and 42-50 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Stein et al., Nucleic Acids Research 16(8):3209-3221 (1988).

In the Office Action (page 3), the Examiner stated that "Stein et al. discloses phosphorothioate linkage modified oligomers for antisense usage but also includes oligomers wherein some of the linkages are of the natural type of phosphodiester."

The anticipation rejection is respectfully traversed.

Applicants respectfully maintain that the instant invention can be distinguished over the cited Stein et al. publication by one or more material elements. Accordingly, reconsideration and withdrawal of the anticipation rejection is respectfully requested.

The Rejection Under 35 U.S.C. §103(a)

Claims 1-51 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Walder et al, PNAS 85:5011-5015 (1988)]in view of Miller et al. (U.S. Patent No. 4,469,863) and Inoue et al., Nucl. Acids Symposium Series 18:958-976 (l988). (Office Action, pages 3-4).

The Examiner's grounds for the rejection was recited given in the Office Action mailed on 6/5/92 in connection with the parent application, (Serial No. 07/446,235), in which action the Examiner stated: (pages 3-5:

> "Walder et al. discloses that the most important element in the efficacy of antisense oligomers inhibiting mRNA expression isthe formation of a RNAse sensitive RNA-DNA duplex that is cleaved by the enzyme: "An important corollary of our results is that such modified analogs must not only retain normal hybridization properties but should also form substrates that are recognized and cleaved by RNAse H (page 5015, second column, second paragraph)..
>
> Miller et al. discloses antisense oligomers with all methylphosphonate internucleotide linkages. These modified oligomers possess resistance to nucleases, can pass through the membranes of mamalian cells, and can form stable duplexes with complementary mRNA (page 769, "Summary").
>
> Inoue et al. teaches that a span as small as three contiguous phosphodiester linakages flanked by modified nucleotides (2'-0-methyl) was capable of forming an RNAse H-sensitive substrate (page 222, first paragraph).
>
> The claimed modified oligonucleotides possess three primary characteristics: 1) endo- and exonuclease resistance, 2) ability to hybridize to its RNA complementary sequence, and 3) the ability for form a RNAse sensitive Rna-DNA duplex.
>
> The person of ordinary skill in the art with the above references before him would have found the claimed modified oligomers obvious because of the necessity to have reduced the number of methylphosphonate internucleotide bonds in the oligomer in order ot make the RNA-DNA duplex RNAse sensitive as Walder et al. emphasizes is critical to the efficacy of antisense oligonucleotides in inhibiting the express of mRNA.
>
> The claimed methods of inhibiting the function of an RNA by contacting said RNA with a nuclease resistant antisense oligomer that forms RNAse H sensitive duplexes with said RNA would also have been obvious in view of the above references that, as a whole, teach the same method.

Finally, the method for identifying modified antisense oligomers possessing the combination of nuclease resistance and theability to form an RNAse H substrate with complexes of RNA using gell electrophoresis instead of the release of acid soluble radioactivity as taught by Walder et al. (page 5012, "RNAse H Assay") would also have been obvious to the person of ordinary skill in the art. the use of gel electrophoresis is a fundamental tool in molecular biology for separating different types of polynucleotides whether by size or by other physical properties such as single-stranded versus double-stranded forms, linear versus circular forms, etc.

The applicant's basic invention is the antisense oligomer with only a portion of the internucleotide linkages or bases modified in order to make the oligomer nuclease reistant. However, the prior art clearly teaches the necessity of combining both nuclease resistance with the ability to form RNAse H sensitive duplexes with RNA. The applicant's gell assay is only one way to assay for RNAse H sensitivity as Walder et al. substantiates."

The obviousness rejection is respectfully traversed.

Applicants respectfully maintain that the differences between the instant invention and the combination of cited documents would not have been obvious to one of ordinary skill in the art at the time of invention.

Reconsideration and withdrawal of the obviousness rejection is respectfully requested.

Applicants acknowledge with appreciation the Examiner's indication that art considered and made of record in the parent application (Serial No. 07/446,235) have also been considered and are made of record herein.

* * * * * *

SUMMARY AND CONCLUSIONS

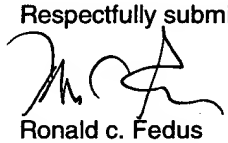
Claims 1-51 are presented for further examination.

This response is being accompanied by a Request For An Extension of Time (Three-Months) Under 37 C.F.R. §1.136(a) and a Request Under 37 C.F.R. §1.129(a) For Withdrawal Of The Finality Of The August 5, 1997 Office Action.

No fee is deemed necessary in connection with the filing of this Response, other than the fees under 37 C.F.R. §1.17(r) for the withdrawal of the finality of the August 5, 1997 Office Action and the fee for the request for the three-month extension of time under 37 C.F.R. §1.17(d). If any fee is due, however, for this response or the accompanying filings, The Patent and Trademark is authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, and to credit any overpayment thereto.

Applicants respectfully submit that all of the instant claims are in allowable condition. Should it be deemed helpful or necessary, the Examiner is respectfully invited to telephone the undersigned at (212) 583-0100 to discuss the subject application.

Respectfully submitted,



Ronald c. Fedus
Registration No. 32,567
Attorney for Applicants

ENZO DIAGNOSTICS, INC.
c/o Enzo Biochem, inc.
527 Madison Avenue, 9th Floor
New York, New York 10017
Tel.: (212) 583-0100
Fax.: (212) 583-0150

lc\uspros\enz47\enz47(c)\AmendmentEnz47C2